937,726

PATENT SPECIFICATION

NO DRAWINGS

937,726

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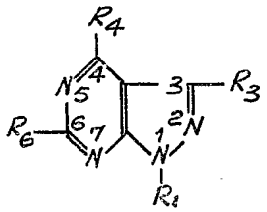
COMPLETE SPECIFICATION

New 4-Mercapto-Pyrazolo[3,4-D]Pyrimidines and process for preparing same

We, CIBA LIMITED, a body corporate organised according to the laws of Switzerland, of Basle, Switzerland, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to new 4-mercapto-pyrazolo[3,4-d]pyrimidines, process for their manufacture and pharmaceutical preparations containing them.

The present invention provides pyrazolo-(3,4-d)pyrimidines of the formula



and their tautomers, and quaternary ammonium compounds or salts thereof.

In the above formula R_1 represents an alkyl, cycloalkyl or cycloalkyl-alkyl group, especially a lower alkyl group. Examples of such substituents are: methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl-(1), pentyl-(2), pentyl-(3), 2-methyl-butyl-(3) or hexyl radicals, cyclopentyl or cyclohexyl radicals, or cyclopentyl- or cyclohexyl-methyl, -ethyl or -propyl radicals.

R_3 represents a hydrogen atom, or secondly a lower alkyl group, for example one of those mentioned for R_1, especially the methyl group.

R_4 is a free mercapto group or a mercapto group substituted by a lower alkyl or an aminoalkyl group. Lower alkyl groups are more especially methyl, ethyl, straight or branched propyl, butyl, pentyl or hexyl groups which may be bound in any position; as aminoalkyl groups there come into consideration more especially those in which the alkyl group separates the sulphur atom from the nitrogen atom by at least 2 carbon atoms and is one of those mentioned above, and in which the amino group is mono- or di-substituted by hydrocarbon groups which may also be interrupted in the chain by oxygen, nitrogen or sulphur. R_4 is therefore, for example a mono- or di-lower alkylaminoethyl, -propyl or -butyl-mercapto group, a pyrrolidinoethyl, -propyl or -butyl-mercapto group, a piperidinoethyl, -propyl or -butyl-mercapto group, a morpholinoethyl, -propyl or -butyl-mercapto group, or a piperazinoethyl, -propyl or -butyl-mercapto group.

R_6 is a lower alkyl group, for example one of those mentioned above in connection with R_4, or an aralkyl group, with the proviso that in a 1:6-dialkyl compound at least one of the alkyl groups in the 1- and 6-positions contains more than 2 carbon atoms. The alkyl groups of the aralkyl groups are more especially, for example, methyl, ethyl, propyl or butyl groups. Besides being a lower alkyl group, R_6 is, for example, a phenylalkyl group, such as a 1- or 2-phenyl-ethyl, 1-phenyl-propyl or phenylmethyl group in which the aromatic nuclei may bear substituents, such as lower alkyl or free or substituted hydroxy, amino or mercapto groups, halogen atoms, trifluoromethyl or nitro groups. The substituents in the aforesaid substituted hydroxy, mercapto or amino groups are more especially of the kind specified above, particularly lower alkyl groups, these groups therefore being, for example, methoxy, ethoxy, propoxy, butoxy, corresponding alkyl-mercapto groups, alkylenedioxy, for example methylenedioxy groups, mono- or di-alkyl-

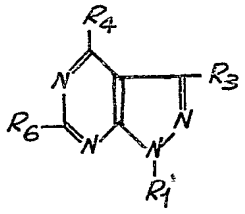
[*Price 4s. 6d.*]

amino groups, for example mono- or dimethylamino, -ethylamino, -propylamino, -butylamino or -pentylamino groups. Halogen atoms are more especially, fluorine, chlorine or bromine. The alkyl radicals of the aralkyl groups may also be substituted, for example by one of the aforementioned aryl or heterocyclic radicals, for example as in the diphenylmethyl radical. In quaternary ammonium compounds there are additional substituents or the tertiary amino group, more especially lower alkyl groups or aralkyl groups, such as the aforementioned benzyl or phenylethyl groups.

The term "lower" in qualifying the hydrocarbon groups is used herein to mean those groups containing up to 7 carbon atoms.

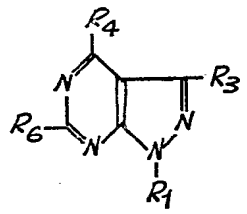
The new compounds have valuable pharmacological properties. More especially they have a coronary dilating effect. The new compounds can consequently be used as medicaments, particularly for the treatment of circulatory disturbances of the myocardium, but also as intermediate products for the preparation of such medicaments. With respect to the use as coronary-dilating agents the aforesaid 1,6-dialkyl compounds are superior to compounds in which each of the two alkyl groups in positions 1 and 6 contains less than 3 carbon atoms.

Of special value are compounds of the formula

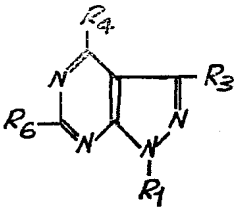


and, if desired, the salts thereof, in which R_1 represents lower alkyl, for example methyl, ethyl, propyl, isopropyl, butyl-(2), 3-methylbutyl-(2), pentyl-(2), pentyl-(3), cycloalkyl, for example cyclopentyl or cyclohexyl, and R_3 stands for hydrogen or lower alkyl and R_6 for an aralkyl group, such as a phenylalkyl group, more especially a phenylmethyl group in which the aryl groups may be unsubstituted or mono-, di- or tri-substituted by halogen, such as chlorine or bromine, alkoxy, such as methoxy or ethoxy, alkyl, such as methyl, ethyl, propyl, isopropyl, butyl, tertiary butyl, methlenedioxy, trifluoromethyl, nitro or amino groups and in which R_4 is a free mercapto group or a mercapto group substituted, for example, as defined above.

Furthermore there are of importance the compounds of the formula

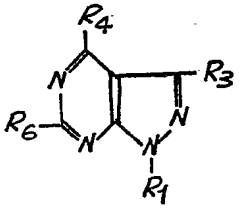


and, if desired, their salts, in which R_1, R_3 and R_4 have the meanings given above and R_6 represents an alkyl group having more than 2 carbon atoms, for example propyl, isopropyl, butyl, isobutyl, amyl or isoamyl, and compounds of the formula



and, if desired, their salts, in which R_3 and R_4 have the meanings given above, R_6 represents methyl or ethyl and R_1 a cycloalkyl group, such as cyclopentyl or cyclohexyl or more especially an alkyl group having at least 3 carbon atoms, such as isopropyl, butyl-(2), pentyl-(2) or pentyl-(3).

Of particular value are the compounds of the formula

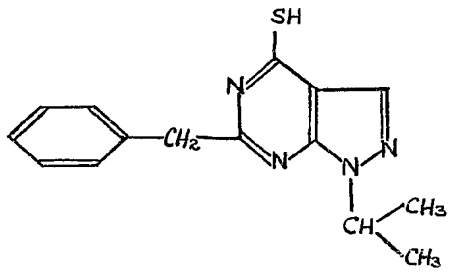


and their salts, in which R_1 has the meaning given above and R_4 represents a lower alkyl group, R_3 a lower alkyl group or more especially hydrogen and R_6 an unsubstituted benzyl group or a benzyl group mono-, di- or tri-substituted in the phenyl radical by chlorine, methoxy, methylenedioxy, methyl or trifluoromethyl.

In these different, preferred groups of compounds R_4 represents above all a free mercapto group or a lower alkyl-mercapto group, such as a methyl-mercapto, ethyl-mercapto, propylmercapto or butylmercapto group.

The present invention relates more especially to the excellent coronary dilatator, 1-isopropyl-

4 - mercapto - 6 - benzylpyrazolo[3,4 - d]-pyrimidine of the formula



and also to the excellent coronary dilatator, 1-isopropyl - 4 - mercapto - 6 - methyl-pyrazolo[3,4-d]pyrimidine, and their salts.

The new compounds are obtained when in a 1 - R_1 - 3 - R_3 - 6 - R_6 - 4 - X - pyrazolo-[3,4-d]pyrimidine, in which X represents a reactive esterified hydroxyl group, for example a halogen atom, such as chlorine, or a free hydroxyl group, and R_1, R_3 and R_6 have the meanings given above, X is converted into the mercapto group R_4 in the conventional manner. The free hydroxyl group may be converted into a mercapto group by treatment with phosphorus pentasulphide, or a halogen atom may be exchanged for a free mercapto group or an alkylmercapto or amino-alkyl-mercapto group, for example by treatment with thiourea, a metal salt of hydrogen sulphide or of an alkyl-mercaptan or amino-alkyl-mercaptan.

The 4-halogeno-pyrazolo[3,4-d]pyrimidines used as starting materials in the present process are obtained by treating a corresponding 4-hydroxy-compound with a halogenating agent, more especially a phosphorus halide, such as phosphorus oxychloride or phosphorus pentachloride.

In a resulting compound containing a free mercapto group or in their tautomers the tautomerizing hydrogen atom may be alkylated or aminoalkylated in the usual manner, for example with a reactive ester of an alcohol. Reactive esters suitable for this purpose are those of hydrochloric, hydrobromic or hydriodic acids, sulphuric acid or an aryl-sulphonic acid; suitable alcohols are more especially lower alkanols or aminoalkanols.

The above reactions are carried out in the conventional manner, preferably at a raised temperature, in the absence or presence of a diluent and/or condensing agent, under atmospheric or superatmospheric pressure.

The invention also includes any modification of the process in which an intermediate obtained at any stage of the process is used as starting material and the remaining steps are carried out, or the process is discontinued at any stage, or in which the starting materials are formed during the reaction, or a necessary substituent is introduced at any stage of the reaction. A resulting tertiary amine may be quaternated in the usual manner, for example with a reactive ester, for example one of those mentioned above, of an alkanol or a phenyl-alkanol.

Depending on the substituents present in the final products, various salts can be prepared therefrom. When they contain acidic mercapto groups, metal salts may be prepared, for example by dissolution in an alkali solution. Compounds of basic nature form salts with inorganic or organic acids. Suitable salt-forming acids are, for example, those which are therapeutically useful, such as hydrohalic acids, sulphuric acids, phosphoric acids, nitric acid, perchloric acid; aliphatic, alicyclic, aromatic or heterocyclic carboxylic or sulphonic acids, such as formic, acetic, propionic, oxalic, succinic, glycollic, lactic, malic, tartaric, citric, ascorbic, hydroxymaleic, dihydroxy-maleic or pyruvic acid; phenyl-acetic, benzoic, para-aminobenzioc, anthranilic, para-hydroxy-benzoic, salicyclic, or para-aminosalicyclic, methane-sulphonic, ethanesulphonic, hydroxy-ethane-sulphonic, ethylene-sulphonic acid; toluene-sulphonic, naphthalenesulphonic acids or sulphanilic acid; methionine, tryptophan, lysine, arginine, cystein or glutamic acid. A resulting salt may be converted in the usual manner into its free base, or a free base into a salt thereof.

The new, pharmacologically valuable compounds, their salts or suitable mixtures thereof can be used, for example in the form of pharmaceutical preparations which contain the aforementioned compounds in admixture or conjunction with an inorganic or organic excipient suitable for enternal, parenteral or local administration. Suitable excipients are substances that do not react with the aforesaid compounds, for example gelatine, lactose, starches, magnesium stearate, talc, vegetable oils, water, benzyl alcohols, gums, poly-alkyleneglycols, cholesterol or any other known pharmaceutical excipient. The pharmaceutical preparations may be in the form of, for example, tablets or dragees, or in liquid form, solutions, suspensions or emulsions. They may be sterilized and/or contain assistants, such as preseratives, stabilisers, wetting or emulsifying agents. They may also contain other therapeutically useful substances. The preparations are obtained by the usual methods. They contain 5—100 mg of the active substance per dosage unit and about 1—70% of active substance.

The 4-hydroxy-compounds used for the manufacture of the 4-mercapto compounds have been described in our Applications Nos. 17102/61, 17105/61 and 17104/61 (Serial Nos. 937,722, 937,724 and 937,723) or are obtained in an analogous manner, for example

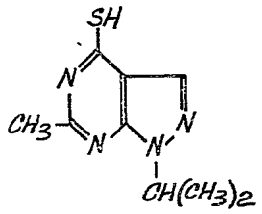
by condensing a 2 - R_1 - 3 - amino - 5 - R_2-pyrazole - 4 - carboxylic acid alkyl ester with a nitrile of the formula R_6—CN in the presence of sodium.

Starting materials preferably used in the present process are those which yield the final products described above as being particularly valuable. The starting materials may also be used in the form of their salts. They are obtained in a manner known *per se*.

The following Examples illustrate the invention:

EXAMPLE 1.

A solution of 18.2 grams of 1 - isopropyl-4 - hydroxy - 6 - methyl - pyrazolo[3:4-d]-pyrimidine in 200 cc of pyridine is treated with 30 grams of phosphorus pentasulphide and the mixture is heated for 8 hours at the boil. The reaction solution is poured into 3 litres of ice water, kept overnight and the yellow precipitate is suctioned off on the following morning. Recrystallization from ethanol yields 1 -isopropyl - 4 - mercapto-6 - methyl - pyrazolo[3:4-d]pyrimidine of the formula



in crystals melting at 226—228°C.

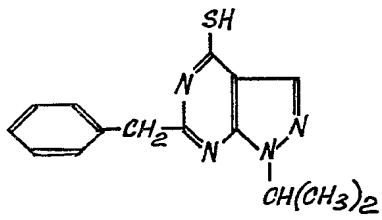
The starting material may be prepared as described in our copending application No. 17104/61 (Serial No. 937,723).

EXAMPLE 2.

A solution of 20.8 grams of 1 - isopropyl-4 - mercapto - 6 - methyl - pyrazolo [3:4-d]-pyrimidine in 130 cc of 2N-sodium hydroxide solution is treated with 24 cc of dimethyl sulphate, stirred for one hour at room temperature and kept overnight. The precipitate is suctioned off and crystallized from petroleum ether, to yield 1 - isopropyl - 4 - methylmercapto - 6 - methyl - pyrazolo[3:4-d]-pyrimidine in yellowish crystals melting at 66—67°C.

EXAMPLE 3.

A solution of 13 grams of 1 - isopropyl-4 - hydroxy - 6 - benzyl - pyrazolo[3:4-d]-pyrimidine in 100 cc of pyridine is treated with 15 grams of phosphorus pentasulphide and the whole is heated at the boil for 8 hours. The reaction solution is then poured into 2 litres of ice water, kept overnight and the yellow precipitate is suctioned off. Recrystallization from a small amount of ethanol yields 1 - isopropyl - 4 - mercapto - 6 - benzyl-pyrazolo[3:4-d]pyrimidine of the formula



in yellow crystals melting at 145—147°C.

The starting material may be prepared as described in our copending application No. 17102/61 (Serial No. 937,722).

EXAMPLE 4.

7 Grams of 1 - isopropyl - 4 - mercapto-6 - benzyl - pyrazolo[3:4-d]pyrimidine are added to a sodium ethylate solution prepared from 0.6 gram of sodium and 150 cc of anhydrous ethanol. To form the sodium salt the mixture is stirred for one hour at room temperature, then treated with 3.5 grams of 2 - chloroethyl - diethylamine, heated for 4 hours at the boil and evaporated to dryness in vacuum; the residue is dissolved in 100 cc of N-hydrochloric acid, adjusted with sodium hydroxide solution to pH 10 and the precipitated oil is taken up in ether. The ether residue is mixed with alcoholic hydrochloric acid which is then evaporated and the residue is recrystallized from ethyl acetate, to yield the hydrochloride of 1 - isopropyl - 4 - (β-diethylaminoethyl mercapto) - 6 - benzyl-pyrazolo[3:4-d]pyrimidine in crystals melting at 160°C.

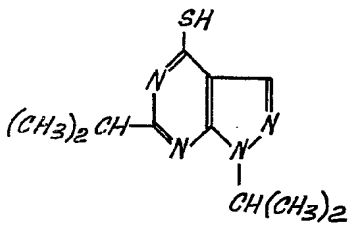
EXAMPLE 5.

A solution of 14 grams of 1 isopropyl - 4-mercapto - 6 - benzyl - pyrazolo[3:4-d]-pyrimidine in 60 cc of 2N-sodium hydroxide solution is treated with 13 grams of dimethyl sulphate and stirred for 2 hours at room temperature. The alkaline solution is then extracted with ether and the ether residue is recrystallized from petroleum ether, to yield 1 - isopropyl - 4 - methylmercapto - 6-benzyl - pyrazolo[3:4-d]pyrimidine in crystals melting at 84—85°C.

EXAMPLE 6.

A solution of 11 grams of 1:6 - diisopropyl-4 - hydroxy - pyrazolo[3:4-d]pyrimidine in 100 cc of pyridine is treated with 15 grams of phosphorus pentasulphide and the mixture is heated at the boil for 8 hours. The reaction solution is then poured into 2 litres of ice water, kept overnight and the yellow precipitate is suctioned off. Recrystallization from isoproyl ether yields 1:6 - diisopropyl-

4 - mercapto - pyrazolo[3:4-d]pyrimidine of the formula



in yellow crystals melting at 170—171°C.

The starting material may be prepared as described in our copending application No. 17104/61 (Serial No. 937,723).

EXAMPLE 7.

A solution of 23.6 grams of 1:6 - diisopropyl - 4 - mercapto - pyrazolo[3:4-d]-pyrimidine in 120 cc of 2N-sodium hydroxide solution is treated with 12.6 grams of dimethyl sulphate and stirred for 2 hours at room temperature. The alkaline solution is then extracted with ether and the residue is distilled. 1:6 - Diisopropyl - 4 - methylmercapto - pyrazolo[3:4-d]pyrimidine passes over between 106 and 109°C under a pressure of 0.05 mm Hg.

EXAMPLE 8.

11.8 Grams of 1:6 - diisopropyl - 4-mercapto - pyrazolo[3:4-d]pyrimidine is added to a sodium ethylate solution prepared from 1.15 grams of sodium and 400 cc of ethanol. To form the sodium salt the mixture is stirred for one hour at room temperature, then treated with 7 grams of β-diethylaminoethyl chloride, heated for 4 hours at the boil, and evaporated to dryness under vacuum. The residue is dissolved in 100 cc of N-hydrochloric acid, the acid solution is extracted with ether, the hydrochloric solution is adjusted with sodium hydroxide solution to pH 10 and the precipitated oil is taken up in ether. The ether residue is distilled. 1:6 - Diisopropyl - 4 - (β - diethylaminoethylmercapto)-pyrazolo[3:4-d]pyrimidine passes over at 138—140°C under a pressure of 0.05 mm Hg.

EXAMPLE 9.

11.8 Grams of 1:6 - diisopropyl - 4-mercapto - pyrazolo[3:4-d]pyrimidine are added to a sodium ethylate solution prepared from 1.15 grams of sodium and 400 cc of ethanol. To form the sodium salt the mixture is stirred for one hour at room temperature, then treated with 7.8 grams of γ-diethylaminopropyl chloride, heated for 4 hours at the boil and evaporated to dryness under vacuum. The residue is dissolved in 100 cc of N-hydrochloric acid, the acid solution is extracted with ether, the hydrochloric solution is adjusted with sodium hydroxide solution to pH 10 and the precipitated oil is taken up in ether. The ether residue is distilled. 1:6-Diisopropyl - 4 - (γ - diethylaminopropylmercapto) - pyrazolo[3:4-d]pyrimidine passes over at 149—151°C under a pressure of 0.02 mm Hg.

EXAMPLE 10.

11.8 Grams of 1:6 - diisopropyl - 4-mercapto - pyrazolo[3:4-d]pyrimidine are added to a sodium ethylate solution prepared from 1.15 grams of sodium and 400 cc of ethanol. To form the sodium salt the mixture is stirred for one hour at room temperature, then treated with 7.7 grams of β-piperidinoethyl chloride, heated for 4 hours at the boil and evaporated to dryness under vacuum. The residue is dissolved in 100 cc of N-hydrochloric acid, the acid solution is extracted with ether, the hydrochloric solution is adjusted with sodium hydroxide solution to pH 10 and the precipitated oil is taken up in ether. The ether residue is distilled. 1:6 - Diisopropyl-4 - (β - piperidinoethylmercapto) - pyrazolo-[3:4-d]pyrimidine passes over at 155—157°C under a pressure of 0.02 mm Hg. The hydrochloride prepared therefrom melts at 163—165°C.

EXAMPLE 11.

11.8 Grams of 1:6 - diisopropyl - 4-mercapto - pyrazolo[3:4-d]pyrimidine are added to a solution ethylate solution prepared from 1.15 grams of sodium and 400 cc of ethanol. To form the sodium salt the mixture is stirred for one hour at room temperature, then treated with 5.7 grams of β - dimethylamino-ethyl chloride, heated for 4 hours at the boil and evaporated to dryness *in vacuo*. The residue is dissolved in 100 cc of N-hydrochloric acid, the acid solution is extracted with ether, the hydrochloric solution is adjusted with sodium hydroxide solution to pH 10 and the precipitated oil is taken up in ether. The ether residue is distilled. 1:6-Diisopropyl - 4 - (β - dimethyl - aminoethylmercapto) - pyrazolo[3:4-d]pyrimidine passes over at 129—130°C under a pressure of 0.05 mm Hg. The hydrochloride prepared therefrom melts at 178—180°C.

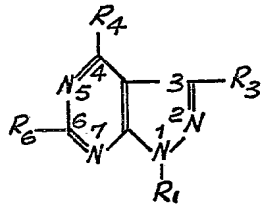
EXAMPLE 12.

1 - Isopropyl - 4 - mercapto - 6 -benzyl-pyrazolo - [3:4-d] - pyrimidine is made up in the usual manner into tablets containing:

1 - isopropyl - 4 - mercapto - 6-benzyl - pyrazolo - [3:4-d]-pyrimidine	10	mg
Lactose	35	mg
Non-swellable starch	20	mg
Wheat starch	10	mg
"Aerosil" — (Registered Trade Mark)	10	mg
Arrowroot	12	mg
Magnesium stearate	0.5	mg
Talc	6	mg

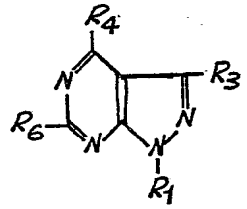
WHAT WE CLAIM IS:—

1. A pyrazolo[3,4-d]pyrimidine of the formula



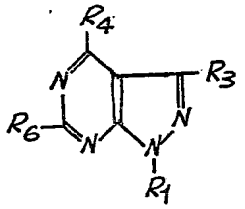
or a tautomer thereof, in which R_1 represents an alkyl, cycloalkyl or cycloalkyl-alkyl group, R_3 represents a hydrogen atom or a lower alkyl group, R_4 represents a free mercapto group or a mercapto group substituted by a lower alkyl or an aminoalkyl group and R_6 represents a lower alkyl or an aralkyl group, with the proviso that in a 1:6 - dialkyl - 3-R_3 - 4 - R_4 - pyrazolo[3,4-d]pyrimidine at least one of the alkyl groups in the 1- and 6-positions contains more than 2 carbon atoms.

2. A compound of the formula



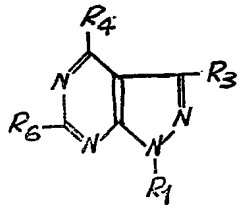
in which R_1 represents a lower alkyl or cycloalkyl group, R_3 represents a hydrogen atom or a lower alkyl group, R_4 represents a free mercapto group or a mercapto group substituted by lower alkyl or aminoalkyl group, and R_6 represents an aralkyl group.

3. A compound of the formula



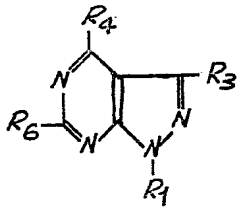
in which R_1, R_3 and R_4 have the meanings given in claim 2, and R_6 represents an alkyl group containing more than 2 carbon atoms.

4. A compound of the formula



in which R_3 and R_4 have the meanings given in claim 2, R_1 represents an alkyl group containing at least 3 carbon atoms, and R_6 represents the methyl or ethyl group.

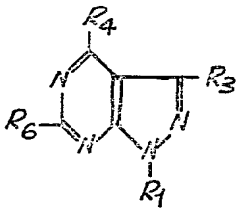
5. A compound of the formula



in which R_3 and R_4 have the meanings given in claim 2, R_1 represents a cycloalkyl group, and R_6 represents the methyl or ethyl group.

6. A compound as claimed in claim 5, in which R_1 represents the cyclopentyl or cyclohexyl group.

7. A compound of the formula



in which R_4 has the meaning given in claim 2, R_1 represents a lower alkyl group, R_3 represents a hydrogen atom or a lower alkyl group and R_6 represents an unsubstituted benzyl group or a benzyl group mono-, di- or tri-substituted in the phenyl radical by chlorine, methoxy, methylene-dioxy, methyl or trifluoromethyl.

8. A quaternary ammonium compound of a compound as claimed in any one of claims 1 to 7.

9. A salt of a compound as claimed in any one of claims 1 to 7.

10. 1 - Isopropyl - 4 - mercapto - 6-benzyl - pyrazolo[3:4-d]pyrimidine.

11. A salt of the compound claimed in claim 10.

12. 1 - Isopropyl - 4 - mercapto - 6-methyl - pyrazolo[3,4-d]pyrimidine.

13. A salt of the compound claimed in claim 12.

14. 1 - Isopropyl - 4 - (methyl - mercapto)-6 - methyl - pyrazolo[3,4-d]pyrimidine.

15. 1 - Isopropyl - 4 - (β - diethylamino-ethylmercapto) - 6 - benzyl - pyrazolo[3,4-d]-pyrimidine.

16. 1 - Isopropyl - 4 - methylmercapto-6 - benzyl - pyrazolo[3,4-d]pyrimidine.

17. 1:6 - Di - isopropyl - 4 - mercapto-pyrazolo[3,4-d]pyrimidine or a salt thereof.

18. 1:6 - Di - isopropyl - 4 - methylmercapto - pyrazolo[3,4-d]pyrimidine.

19. 1:6 - Di - isopropyl - 4 - (β - diethylaminoethylmercapto) - pyrazolo[3,4-d]-pyrimidine.

20. 1:6 - Di - isopropyl - 4 - (γ - diethylaminopropylmercapto) - pyrazolo[3,4-d]-pyrimidine.

21. 1:6 - Di - isopropyl - 4 - (β-piperidinoethylmercapto) - pyrazolo[3,4-d]-pyrimidine.

22. 1:6 - Di - isopropyl - 4 - (β - dimethylaminoethylmercapto) - pyrazolo[3,4-d]-pyrimidine.

23. A salt of a compound as claimed in any one of claims 14, 15 and 19 to 22.

24. A new compound as claimed in claim 1, or a salt thereof, and described in any one of Examples to 11 herein.

25. A pharmaceutical preparation which comprises a compound as claimed in any one of claims 1 to 7 in admixture or conjunction with a pharmaceutically suitable excipient.

26. A pharmaceutical preparation which comprises a quaternary ammonium compound as claimed in claim 8 in admixture or conjunction with a pharmaceutically suitable excipient.

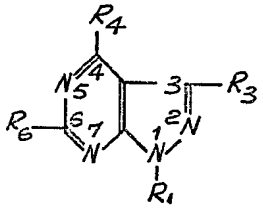
27. A pharmaceutical preparation which comprises a salt as claimed in claim 9 in admixture or conjunction with a pharmaceutically suitable excipient.

28. A pharmaceutical preparation which comprises a compound as defined in claim 1 and claimed in any one of claims 10, 12, 14 to 22 and 24 in admixture or conjunction with a pharmaceutically suitable excipient.

29. A pharmaceutical preparation which comprises a salt as defined in claim 9 and claimed in any one of claims 11, 13, 17, 23 and 24 in admixture or conjunction with a pharmaceutically suitable excipient.

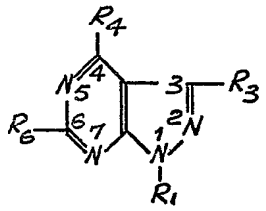
30. A pharmaceutical preparation having the composition substantially as described in Example 12 herein.

31. A process for the manufacture of a mercapto-pyrazolo[3,4-d]pyrimidine of the formula



or a tautomer thereof, in which R_1 represents an alkyl, cycloalkyl or cycloalkyl-alkyl group, R_3 represents a hydrogen atom or a lower alkyl group, R_4 represents a free mercapto group or a mercapto group substituted by a lower alkyl or an aminoalkyl group and R_6 represents a lower alkyl or an aralkyl group, with the proviso that in a 1:6 - dialkyl - 3-R_3 - 4 - R_4 - pyrazolo[3:4-d]pyrimidine at least one of the alkyl groups in the 1- and 6-positions contains more than 2 carbon atoms; or a quaternary ammonium compound or a salt thereof; wherein a 1 - R_1 - 3 - R_3 - 6-R_6 - 4 - X - pyrazolo[3,4-d]pyrimidine, in which X represents a halogen atom and R_1, R_3 and R_6 have the meanings given above, is reacted with thiourea, a metal salt of a hydrogen sulphide or of an alkylmercaptan or aminoalkyl-mercaptan, and, if desired, in a resulting compound with a free mercapto group the latter is converted into a substituted mercapto group R_4 by reaction with a reactive ester of an alkanol or aminoalkanol, and, if desired, a resulting tertiary amine is quaternated and/or a resulting free compound converted into a salt thereof or a resulting salt into the free compound.

32. A process for the manufacture of a mercapto-pyrazolo[3,4-d]pyrimidine of the formula



or a tautomer thereof, in which R_1 represents an alkyl, cycloalkyl or cycloalkyl-alkyl group, R_3 represents a hydrogen atom or a lower alkyl group, R_4 represents a free mercapto group or a mercapto group substituted by a lower alkyl or an aminoalkyl group and R_6 represents a lower alkyl or an aralkyl group, with the proviso that in a 1:6 - dialkyl - 3-R_3 - 4 - R_4 - pyrazolo[3:4-d]pyrimidine at least one of the alkyl groups in the 1- and 6-positions contains more than 2 carbon atoms; or a quaternary ammonium compound or a salt thereof; wherein a 1 - R_1 - 3 - R_3 - 6-R_6 - 4 - hydroxy - pyrazolo[3,4-d]pyrimidine in which R_1, R_3 and R_6 have the meanings given above, is reacted with phosphorus pentasulphide and, if desired, in a resulting compound with a free mercapto group the latter is converted into a substituted mercapto group R_4 by reaction with a reactive ester of an alkanol or aminoalkanol, and, if desired, a resulting tertiary amine is quaternated and/or a resulting free compound converted into a salt thereof or a resulting salt into the free compound.

33. A process for the manufacture of a 4 - mercapto - pyrazolo[3:4-d]pyrimidine conducted substantially as described in any one of Examples 1 to 11 herein.

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